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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/647,088	08/21/2003	Irving Boime	295002005901	1723

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MORRISON & FOERSTER LLP
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EXAMINER	
SPECTOR, LORRAINE	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
07/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/647,088	BOIME ET AL.	
	Examiner	Art Unit	
	Lorraine Spector, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-28* is/are pending in the application.

4a) Of the above claim(s) *24 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-23,25 and 28* is/are rejected.

7)☒ Claim(s) *27* is/are objected to.

8)☒ Claim(s) *21-28* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 21-23, 25 and 27-28 are under consideration. The elected species is that wherein β^1 and β^2 are both FSH agonists. It is noted that the elected species, which occurs in claims 25 and 27, is free of the prior art. However, the generic claims remain rejected.

The rejection of claims 21-23, 25 and 27-28 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of applicants arguments and/or amendments.

The rejection of claims 21-23, and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Sugihara et al., PNAS 92:2041 is withdrawn in view of applicants amendments.

Priority

Priority for the claimed invention is 10/19/1998. The disclosure of the '501 patent, filed 11/17/1997 does not envision the claimed invention.

Terminal Disclaimer

The terminal disclaimer filed on 4/30/2007 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 6,635,256 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Specification

The new title of the invention is acknowledged.

The objection to Claim 21 for encompassing the non-elected invention, wherein there is a covalent linkage was in error, and is withdrawn.

Claims 21-23, 25 and 27-28 are objected to for encompassing non-elected species, there being no allowable generic claim. If allowability of the elected species is determined and the genus remains non-allowable, applicants will be required to amend the claims to limit to the elected species.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 21-23, 25 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over G. De Rosa et al., Annales d'endocrinologie 48(6):468-472, 1987 (Abstract only) in view of either R.K. Hyde et al., Biology of Reproduction 54(Suppl. 1) :105, Abstract 193, 1996. The omission of claim 25 from the previous rejection as inadvertent. Clearly the penultimate member of the Markush group therein was specifically addressed, as this is the species taught by Ben-Menahem. The Ben-Menahem references having been removed, the species is still obvious, for reasons cited below.

This is essentially the same rejection as of record, with the exception that either the Hyde reference alone is sufficient to supplement the teachings of the primary reference, the Ben-

Menahem reference having been removed. With the removal of the Ben-Menahem reference, there is an additional difference between the prior art and the claims, in that the species taught by Hyde et al. is specifically excluded from the claims; it is the reverse combination that is claimed; FSH$\beta\alpha$ covalently linked to hCGα. However; in view of the known and extraordinary conservation in structure among the glycoprotein hormones, and in view of the prosecution in the parent application 08/971439 in which it was determined that a single working embodiment of single-chain hCG was sufficient to enable all single chain glycoprotein hormones (see especially applicants arguments in the Interview Summary document of 2/17/1999), the Examiner finds that the reversal of orientation from that taught by Hyde to that claimed herein is *prima facie* obvious. In fact, any combination of subunits is *prima facie* obvious so long as those subunits are known to be used together. There is no criticality to what specific subunits comprise the single chain hormone portion of the complex, nor what subunit comprises the additional β subunit in view of the art, the parent application, and the instant claims themselves. Accordingly, the invention, taken as a whole, is *prima facie* obvious.

Applicants arguments, filed 4/30/2007 have been fully considered but are not deemed persuasive.

In the previous rejection, the Examiner characterized the Hyde reference thusly:

"Hyde et al. teach that coadministration of hCG$\beta\alpha$ and FSHβ results both hCG and FSH activity."

Applicant argues that the Examiner's interpretation of the reference is not exactly correct, in that as stated by Applicant, "supernatants from CHO cells that express separate constructs... were tested only for receptor binding activity and adenylate cyclase activity." This argument has been fully considered but is not deemed persuasive. The Examiner concedes that she may have slightly mis-characterized the references. The Examiner concurs that Hyde does not teach *administration* of the non-covelently linked complex. This true; however, such is not necessary to anticipate claims 21-23. With respect to claim 28, the primary reference provides motivation to make a pharmaceutically acceptable formulation of the complex produced by Hyde or Ben-Menahem.

Upon re-reading the Hyde reference, the Examiner finds the statement: "Biological assays of media from clones producing this complex show both FSH and hCG activity." The Examiner interprets this sentences as indicating that the complexes were formed in the cells (i.e. *in vivo*), and were "biologically active, meaning that they demonstrated binding and signaling through both receptors. Thus, the person of ordinary skill in the art would have reasonably expected that administration of the complex would provide both activities. Applicants further argue that Hyde further states that "the hCG activity observed may be due to the hCG$\beta\alpha$ tether only", and not the complex. This argument has been fully considered but is not deemed persuasive because it is not relevant. Hyde teaches exactly the same molecule as claimed herein. The properties of the complex are not separable from the complex itself. The References lead to the reasonable expectation that the molecule has both hormone activities; it is not relevant whether the complex is maintained at the exact moment that CG activity is observed. Further, the claims contain no activity limitations.

It is believed that all pertinent arguments have been addressed.

Conclusion

Claim 27 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. There is no motivation in the prior art to combine agonist activity with antagonist activity in the same complex.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

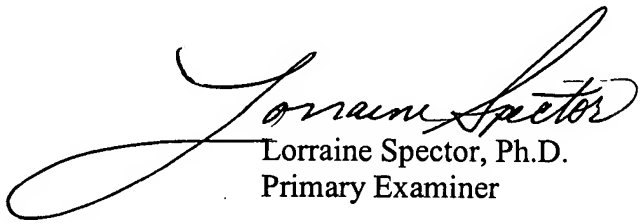
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 3:00 P.M. at telephone number 571-272-0893.

If attempts to reach the Examiner by telephone are unsuccessful, please contact the Examiner's supervisor, Dr. Gary Nickol, at telephone number 571-272-0835.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to **571-273-8300**. Faxed draft or informal communications with the examiner should be directed to ***571-273-0893.***

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Lorraine Spector, Ph.D.
Primary Examiner